



STUDY OF BIOCHEMICAL PROFILE OF GALL STONES IN PATIENTS WITH CHOLELITHIASIS AT A TERTIARY HOSPITAL

General Surgery

**Dr.K.Divya
Bharathy***

Resident, Dept of Surgery, Bharati Vidyapeeth Deemed University Medical College, Pune. * Corresponding Author

Dr.Sudhir Shinde

Professor, Dept of Surgery, Bharati Vidyapeeth Deemed University Medical College, Pune.

Dr.Abhay Kumar

Asst Prof, Dept of surgery, Bharati Vidyapeeth Deemed University Medical college, Pune.

ABSTRACT

Gallstones disease (GD) is a prevalent gastro-intestinal illness that affects people all over the world. Present study was aimed to study the biochemical profile of Cholelithiasis patients. Present study was single-center, cross sectional study, conducted in patients admitted in surgical wards, presence of gallstone was confirmed by ultrasound abdomen & underwent cholecystectomy for the same. Among patient's majority belong to 41-60 years of age (42.4%), & were females (63.6%). Abnormal values of serum cholesterol, Serum Bilirubin, Serum Calcium & Serum Phosphate were noted in 77.3%, 30.3%, 72.7%. 34.8% patients respectively. Majority patients had Cholelithiasis (34.8%), followed by cholelithiasis with cholecystitis (27.3%), calculous cholelithiasis, cholelithiasis without cholecystitis (15.2%), & cholelithiasis with choledocholithiasis (4.5%). Among patients, majority of 33(50%) have cholesterol stones, followed by 22(33.3%) have cholesterol stones and 11(16.7%) had pigment stones. We noted a statistical significance between serum Cholesterol and type of gallstone ($p=0.021$) as well as between serum Phosphate and type of gallstone ($p=0.001$). Cholelithiasis causes a considerable increase in serum cholesterol and serum calcium levels. Risk is increased by a sedentary lifestyle and light physical activity. The most prevalent form of gallstone comprises mixed gallstones.

KEYWORDS

Gall Stones, Cholelithiasis, Cholesterol Stone, Biochemical Study,

INTRODUCTION

Gallstones disease (GD) is a prevalent gastro-intestinal illness that affects people all over the world¹. The major elements which are involved in the formation of gall stones are cholesterol, bile pigments, calcium, hepatic bile composition, biliary glycoprotein, infection, age, sex, genetics, oestrogen, dietary factors, geographical prevalence².

Cholesterol stones had higher quantities of total cholesterol, phospholipids, fatty acids (esterified), inorganic phosphate, and copper than mixed and coloured stones. Gallstones of black and brown pigment are physically, chemically, and clinically unique. In sterile bile, black stones grow in the gallbladder and are linked to advanced age, chronic hemolysis, alcoholism, cirrhosis, pancreatitis, and complete parenteral nutrition.³

Local gallbladder variables alter the precipitation of calcium carbonate and phosphate. In bile infected with enteric bacteria that produce hydrolytic enzymes such as beta-glucuronidase, phospholipase A, and conjugated bile acid hydrolase, brown pigment stones occur. Bilirubin and fatty acid anions generate insoluble calcium salts as a result of this reaction. The existence of 40% bilirubin monoconjugates in mouse gallstones showed that this moiety is important in the development of black gall stones.⁴ Present study was aimed to study the biochemical profile of Cholelithiasis patients.

MATERIAL AND METHODS

Present study was single-center, cross sectional study, conducted in department of general surgery, at Bharati Vidyapeeth (deemed to be university), Pune, India. Study duration was of 2 years (August 2019 to August 2021). Study was approved by institutional ethical committee.

INCLUSION CRITERIA

- Patients admitted in surgical wards, presence of gallstone was confirmed by ultrasound abdomen & underwent cholecystectomy for the same

EXCLUSION CRITERIA

- Acalculous Cholecystitis
- Patients with obstructive Jaundice.
- Patients who were not fit for cholecystectomy.
- Patients who refused cholecystectomy.

clinical details (history, examination), laboratory investigations (serum cholesterol, bilirubin, phosphate and calcium), radiological findings, intraoperative findings were noted in case record proforma.

Patients after cholecystectomy and retrieval of stones, were divided into three groups based on the morphology of gallstones into

1. Whitish to pale yellow as cholesterol stones.
2. Black to blackish brown as pigment stones.
3. Yellow brown and greenish white as mixed stones.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

Among patient's majority belong to 41-60 years of age 28(42.4%), followed by 21-40 years of age 27(40.9%), majority were females 42(63.6%). 28(42.4%) were healthy, 16(24.2%) were underweight, 15(22.7%) were overweight and 7(10.6%) were obese. Among Patients, 25(37.9%) had diabetes & 25(37.9%) had hypertension.

Table 1: Age & gender distribution

Characteristic	Frequency	Percent
Age (Years)		
<20	1	1.5
21-40	27	40.9
41-60	28	42.4
>60	10	15.2
Gender		
Males	24	36.4
Females	42	63.6
BMI		
<18.5	16	24.2
18.5-24.9	28	42.4
25-29.9	15	22.7
>30	7	10.6
Life style		
Sedentary	15	22.7
Light activity	23	34.8
Moderate activity	22	33.3
Heavy activity	6	9.1
Co-morbidities		
Diabetes	25	37.9
Hypertension	22	33.3

Abnormal values of serum cholesterol, Serum Bilirubin, Serum Calcium & Serum Phosphate were noted in 77.3%, 30.3%, 72.7%. 34.8% patients respectively.

Table 2- Laboratory investigations

Laboratory investigations	Values (Mean $\pm$ SD)	Normal	Abnormal
Serum Cholesterol	254.62 $\pm$ 66.05	15 (22.7 %)	51 (77.3 %)
Serum Bilirubin	1.22 $\pm$ 0.61	46 (69.7 %)	20 (30.3 %)
Serum Calcium	11.1 $\pm$ 1.52	18 (27.3 %)	48 (72.7 %)
Serum Phosphate	4.03 $\pm$ 0.99	43 (65.2 %)	23 (34.8 %)

Majority patients had Cholelithiasis (34.8%), followed by cholelithiasis with cholecystitis (27.3%), calculous cholelithiasis, cholelithiasis without cholecystitis (15.2%), & cholelithiasis with choledocholithiasis (4.5%).

Table 3: Ultrasound Diagnosis

USG Diagnosis	Frequency	Percent
Cholelithiasis	23	34.8
Calculous Cholecystitis	12	18.2
Cholelithiasis with Cholecystitis	18	27.3
Cholelithiasis without Cholecystitis	10	15.2
Cholelithiasis with choledocholithiasis	3	4.5

Among patients, majority of 33(50%) have cholesterol stones, followed by 22(33.3%) have cholesterol stones and 11(16.7%) had pigment stones. Among patients, majority have yellow-coloured stones 21(31.8%), followed by 14(21.2%) white colour, 12(18.2%) greenish white colour, 8(12.1%) pale yellow colour, 7(10.6%) black colour and 4(6.1%) had blackish brown colour.

Table 4: Stone Characteristic

Characteristic	Frequency	Percent
Type of gallstones		
Cholesterol stones	22	33.3
Pigment Stones	11	16.7
Mixed stones	33	50.0
Colour of stone		
Black	7	10.6
Blackish brown	4	6.1
Greenish white	12	18.2
Pale yellow	8	12.1
White	14	21.2
yellow brown	21	31.8

Among Mixed gallstone patients, cholelithiasis (42.4%) & calculous cholecystitis (21.2%) were common causes. Among Pigment gallstone patients, cholelithiasis (36.4%) & cholelithiasis with cholecystitis (36.4%) were common causes. Among Cholesterol gallstone patients, cholelithiasis (22.7%) & cholelithiasis without cholecystitis (22.7%) were common causes. There were no statistical association between Diagnosis and type of gallstone.

Table 5: USG Diagnosis and type of gallstone

USG diagnosis	Cholesterol stones (n=22)	Pigment stones (n=11)	Mixed gallstones (n=33)	P value
Cholelithiasis	5(22.7%)	4(36.4%)	14(42.4)	0.356
Calculous Cholecystitis	4(18.2%)	1(9.1%)	7(21.2%)	
Cholelithiasis with Cholecystitis	8(36.4%)	4(36.4%)	6(18.2%)	
Cholelithiasis without Cholecystitis	5(22.7%)	2(18.2%)	3(9.1%)	
Cholelithiasis with choledocholithiasis	0	0	3(9.1%)	

In present study, we noted a statistical significance between serum Cholesterol and type of gallstone (p=0.021) as well as between serum Phosphate and type of gallstone (p=0.001).

Table 6: Type of gallstone & Laboratory investigations

Laboratory investigations	Serum levels	Cholesterol stones	Pigment stones	Mixed gallstones	P value
Serum cholesterol	Normal	3(13.6%)	0	12(36.4%)	0.021
	Abnormal	19(86.4%)	11(100%)	21(63.3%)	
Serum Bilirubin	Normal	15(68.2%)	8(72.7%)	23(69.7%)	0.965
	Abnormal	7(31.8%)	3(27.3%)	10(30.3%)	
Serum Calcium	Normal	6(27.3%)	0	12(36.4%)	0.064
	Abnormal	16(72.7%)	11(100%)	21(63.6%)	

Serum	Normal	12(54.5%)	2(18.2%)	29(87.9%)	0.0001
Phosphate	Abnormal	10(45.5%)	9(81.8%)	4(12.1%)	

DISCUSSION

Gall-stone disease is a multifaceted illness. Gender is one of the most key risk factors for GD in the general population: gallstones are more prevalent in women than in men. Other considerations comprise age, genetics, and race. Additional factors include obesity, fast weight loss, glucose intolerance, insulin resistance, a high dietary glycemic load, alcohol usage, diabetes, hypertriglyceridemia, medications, and pregnancy. There are four major types of factors that all play a role in the production of cholesterol gallstones to some extent:^{7,8}

- 1) bile cholesterol supersaturation;
- 2) cholesterol precipitation and crystallisation core creation;
- 3) basic gallbladder activities (contraction, absorption, secretion, and so on);and
- 4) those that impair bile acid enterohepatic circulation.^{7,8}

Study done by Shashidar KN et al.,⁹ there is more Cholelithiasis patients among 41-50 years of age and the findings are consistent with our study. A study done by Kurtin WE et al.,¹ decrease in gallstones formation after age of 50 and increase in chance of gall stones on young age was noted. In our study on the contrary there is more Cholelithiasis patients, among 41 -60 years followed by 21-40 years and least in <20 years.

Among Patients, majority are females 42(63.6%) and 24(36.4%) are males. A study done by Gottfried Novacek et al.,⁹ female gender pregnancy are risk factors for gall stones. In our study about fifty percentage of females have gall stones.

The majority of patients in our current study are healthy, with underweight, overweight, and obese individuals following closely behind. Rapid weight reduction increases the incidence of gallstones, according to a study by Erlinger S et al.,¹⁰. Cholelithiasis patients have higher levels of serum cholesterol in the current study. Al saadi et al.,¹¹ noted that, cholelithiasis patients have a considerable increase in cholesterol levels. Similar findings were noted by Hafiz MA et al.,⁴ Bose SM et al.,¹² Sikandar H et al.,⁹ & present study.

In present study, abnormal Serum Bilirubin levels were noted in 20 (30.3%). Serum bilirubin is a good predictor for gallstone formation but not as consistently strong predictors as Alkaline phosphate. The degree of elevated Serum bilirubin reflects the degree of liver damage.

The present study majority of Cholelithiasis patients (72.7%) there was rise in serum calcium levels. These findings are consistent with study done by Rudnicki M et al.,¹³ & Gleeson D et al.,¹⁴.

Vivek K Singh et al.,¹⁵ shows that majority of Cholelithiasis patients with disease have mixed gall stone as most predominant type to occur. This study's findings are compatible with this study's findings. Study done by Shashidar KN et.,⁹ majority of Cholelithiasis patients have mixed gallstone as a finding. Our findings are compatible with previous research.

In our present study majority of patients, yellow-coloured stones are predominant and least is blackish brown colour. A study done by Vivek K Singh et al.,¹⁵ most predominant colour is yellow colour, white colour. Our findings are compatible with previous research.

Gallstones are categorised predicated on their chemical nature: cholesterol, pigment, and pigment stones. Gallstones in GD are divided into three categories: (1) cholesterol stones, which account for up to 75% of all gallstones; (2) pigment stones; and (3) mixed stones.¹⁶

Histochemical investigations utilising light microscopy provide information on the structural link between glycoproteins and cholesterol in the GS.¹⁷ The principal components of cholesterol GS, according to colour cathodoluminescence scanning electron microscopy (CCLSEM) investigations, are cholesterol and protein ingredients. Individual embeddings of bilirubin are arranged on the surface of a stone piece.¹⁸

Pigments with less than 30% cholesterol are known as GS pigments. These pigment stones are black (small and compact) and brown (big and softer). Gallstones made up of black pigment constitute for 20 percent to 30 percent of all gallstones in GD, and they are more

common in the elderly. They are primarily made up of calcium bilirubinate, phosphate, and carbonate, with no cholesterol.^{19,20}

Brown pigment stones are assumed to be intrahepatic stones (bilirubinarbonate stones). The inclusion of free bile acids in intrahepatic stones was observed, and it was encountered that bacterial infection, which deconjugates the glycine and taurine conjugations, plays a role in the pathogenesis of GS.²²

Because the majority of gall stone patients are asymptomatic, the current study provides an in-depth look at the biochemical analysis of the stones, their occurrence, age and gender distribution, risk factors, stone types, lipid profiles, histological diagnosis, and bile culture.⁵

Limitations of study were small sample size, availability various biochemical tests and cost for stone analysis are the limiting factors in low scale hospital setups & high individual variability of serum biochemical markers levels.

CONCLUSIONS

Cholelithiasis causes a considerable increase in serum cholesterol and serum calcium levels. Risk is increased by a sedentary lifestyle and light physical activity. The most prevalent form of gallstone comprises mixed gallstones.. It is critical to research sociodemographic variables and biochemical components of cholelithiasis from a public health standpoint.

REFERENCES:

1. Kurtin WE, Schwesinger WH, Diehl AK. Age-related changes in the chemical composition of gallstones. *Int J Surg Invest*. 2000;2(4):299-307.
2. Novacek G. Gender and gallstone disease. *Wien Med Wochenschr*. 2006;156(19-20): 527-33.
3. Kard RW. Gallstones, cholecystitis and diabetes. Erratum in: *Surg Gynecol Obstet* 1991 Jul;173(1):72.
4. Hafiz MA et al. Assessment of gallstone predictors: comparative analysis of ultrasonographic and biochemical parameters. *International Archives of medicine*. 2013;6:1-7.
5. Madden AM, Trivedi D, Smeeton NC, Culklin A. Modified dietary fat intake for treatment of gallstone disease. *Cochrane Database Syst Rev*. Mar 22 2017;(3):1-10.
6. Sikandar H et al. Comparative analysis of serum lipid profiles in patients with and without gallstones: A prospective Cross-sectional Study. *Annals of medicine and surgery*. 2019;42:11-13.
7. Stewart L, Griffis JM, Way LM. Spectrum of gall stones disease in the veteran population. *Am J Surg* 1990;190:746-51.
8. Järvinen H. Abnormal liver function tests in acute cholecystitis; the predicting of common duct stones. *Ann Clin Res*. 1978 Dec;10(6):323-7.
9. Shashidar KN, Prasad paul, Mohan KK, Shankar M, Hemalatha A. Risk Factors and the Biochemical Evaluation of Biliary Calculi in Rural Kolar, Karnataka, India: A Rural Perspective of an Urban Disease. *Jurnal of clinical and diagnostic Research*. 2012;6(3): 364-368.
10. Erlinger S. Gallstones in obesity and weight loss. *Eur J Gastroenterol Hepatol*. 2000 Dec;12(12):1347-52.
11. Al-Saadi, Narjis. Biochemical and demographical study of lipid profile in sera of patients with gallstone. *Iraqi Journal of Science*. 2018;53(2):759-767.
12. Bose SM, Mazumdar A, Prakash VS, Kocher R, Katariya S, Pathak CM. Evaluation of the predictors of choledocholithiasis: comparative analysis of clinical, biochemical, radiological, radionuclear, and intraoperative parameters. *Surg Today*. 2001;31(2):117-22.
13. Rudnicki M, Jorgensen T, Skovgaard N, Pedersen IK, Thode J. Lack of relationship between serum and gallbladder bile calcium in patients with gallstone disease. *Scand J Clin Lab Invest*. 2009;58(8):677-82.
14. Gleeson D, Murphy GM, Dowling RH. Changes in serum calcium levels influence biliary calcium levels in humans. *Gastroenterology* 1994; 107: 1812-8.
15. Vivek k singh, Brijbir SJ, Jitendra Sharma, Pradeep KR. Analysis of stones formed in the human gall bladder and kidney using advanced spectroscopic techniques. *International union for pure and applied biophysics*. 2019;12:647-668.
16. Atman M. Study of lipid profile and biliary composition in patient with gallstone. *Baghdad*. 2006.
17. Sohail S, Iqbal Z. Sonographically determined clues to the symptomatic or silent cholelithiasis. *J Coll Physicians Surg Pak*. 2007;17(11):654-657.
18. Garg, KP, Pundir, CS. An extended chemical analysis of gallstone Indian Journal of Clinical Biochemistry. 2007; 22 [2]: 145-150.
19. Pundir CS, Chaudhary R, Rani K, Chandran P, Kumari, M. and Garg, P. Chemical analysis of biliary calculi in Haryana. *Ind. J. Surg*. 2001;63: 370-373.
20. Kumar D, Garg, PK, Tandon RK. Clinical and biochemical comparative study of different types of common bile duct stones. *Ind. J. Gastroenterol*. 2001. 20: 187-90.
21. Amin, AM, Ananthakrishnan N, Nambinarayanan TK. Composition of gallstones and Sequential events in biliary lithogenesis – is it different in South India compared to north? *J. Assoc. Physicians India*. 2001; 48: 885- 90. Bortoff GA, Chen MYM, Ott DJ, Wolfman NT, Routh WD. Gallbladder stones: imaging and intervention. *Radiographs*. 2000; 20:751-766.